Claim 3 was objected to because of an informality. Claim 3 listed features (a)-(f) and (h)-(i), however, feature (g) was not listed. Applicants have amended claim 3 to depend from base claim 1. As the claim structure has changed, the features are no longer alphabetically labelled, and the objection is obviated. Accordingly, Applicants trust that claim 3 is now free from objections due to informalities.

Claim rejections under 35 U.S.C. §112

Claims 64-75 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that claim 64 is unclear whether it is an independent method claim or a method that depends on the apparatus of either claims 1, 2, 3, or 4. Applicants have removed the unclear language, and submit that Claim 64 now clearly indicates that it is an independent method claim. Accordingly, Applicants submit that the 35 U.S.C. §112, second paragraph, rejection of claim 64 should be withdrawn.

The Examiner further suggested that claim 65 contained an improper Markush group in that the steady-state measurement method is totally embraced within the transient measurement group. Without admitting to the impropriety of the Markush group, in order to further prosecution Applicants have amended claim 65 to remove the language the Examiner found objectionable. Applicants request that the 35 U.S.C. §112, second paragraph, rejection of claim 65 be withdrawn.

The Examiner suggested that the acronym 'AC' of claims 65-68 is not defined in the claim so that those who are of ordinary skill in the art would know the intended meaning. In a similar manner, the Examiner suggested that the acronym 'DC' of claim 67 was similarly not defined. Applicants respectfully disagree, and submit that the acronyms 'AC' and 'DC' are readily understood by those skilled in the art. In order to further prosecution, however, Applicants have defined the acronyms as 'alternating current' and 'direct current', respectively, within the claims. Accordingly, Applicants request that the 35 U.S.C. §112, second paragraph, rejection of claims 65-68 be withdrawn.

Claims 65-75 were further rejected under 35 U.S.C. §112, second paragraph, as being dependent on rejected base claim 64. Applicants submit, above, that amended claim 64 now particularly points out and distinctly claims the subject matter which Applicants regard as the invention. Accordingly, Applicants request that the 35 U.S.C. §112, second paragraph, rejection of claim 65-75 be withdrawn.

Claim Rejections - 35 U.S.C. §102

Claims 1-2, 6-30, 33-46, 48-51 and 53-75 were rejected under 35 U.S.C. §102(e) as being anticipated by Kayyem et al. (U.S. Patent Number 6,290,839).

Kayyem discloses an apparatus for detection of analytes comprising two sets of electrodes - an electrophoresis set and a detection set (see Kayyem Figs. 1A-F and col. 2, lines 40-42). The electrophoresis electrodes are employed to manipulate analytes within a sample, and the detection electrodes are utilized to detect target analytes.

In contrast, Applicants' claims 1 and 2 recite "a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site" and "a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site".

As the Examiner is aware, for a reference to anticipate a claim, the reference must teach every element of the claim (see M.P.E.P §2131).

The Examiner suggests that, by disclosing a set of electrophoresis electrodes and a set of detection electrodes, Kayyem has anticipated the electrodes recited in Applicants' claims 1 and 2. However, Applicants submit that amended claims 1 and 2 clearly recite input electrodes arranged "such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site". In an analogous manner, amended claims 1 and 2 further recite output electrodes arranged "such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site". This arrangement is neither taught nor suggested by Kayyem. Claims 6-30, 33-46, 48-51 and 53-63 depend from and include all limitations of claims 1 or 2. Accordingly, Applicants respectfully request that the 35 U.S.C. §102(e) rejection of claims 1-2, 6-30, 33-46, 48-51 and 53-63 over Kayyem be withdrawn.

Further, claim 64 recites "applying a first electrical signal at an input electrode in contact with a first set of porous, polymeric pads, wherein the first set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site," and "detecting the first electrical signal at an output electrode in contact with a second set of porous, polymeric pads, wherein the second set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site". Applicants submit that Kayyem does not disclose or suggest these features. Claims 65-75 depend from and include all limitations of Applicants' claim 64. Accordingly, Applicants respectfully request that the 35 U.S.C. §102(e) rejection of claims 64-75 be withdrawn.

Claim Rejections - 35 U.S.C. §103

Claims 3-75 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kayyem et al. in view of Roberts et al. (U.S. Patent 5,958,791).

Kayyem is discussed above. The Examiner concedes Kayyem does not disclose interdigitated input and output electrodes, as recited in Applicants' claims 3 and 4.

Roberts discloses an apparatus having interdigitated input and output electrodes. One input electrode is interdigitated with one output electrode at each test site (see Roberts Fig. 1 and col. 15, lines 18-32). For a two test site setup (as in Roberts' Fig. 1), two potentiostats are provided - one to connect the input and output electrodes at a first site, and a second to connect the input and output electrodes at a second site.

In contrast, Applicants' amended claims 3 and 4 depend from and include all limitations of Applicants' claims 1 and 2, and clearly recite "a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site" and "a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site".

As the Examiner is aware, to constitute a proper 35 U.S.C. §103 rejection, the cited reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §2142).

The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the apparatus of Kayyem by interdigitating the input and output electrodes as taught by Roberts for the advantage of increasing signal detection. However, Applicants submit that the combination of Kayyem and Roberts fail to disclose or suggest all limitations of Applicants' claims 3 and 4, dependent from claims 1 and 2, including "a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site" and "a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site". Claims 5-63 depend from and include all limitations of claims 3 and 4. Accordingly, Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 3-63 over Kayyem in view of Roberts be withdrawn.

In an analogous manner, Applicants submit that Kayyem and Roberts, taken alone or in combination, fail to disclose all limitations of Applicants' claim 64 including "applying a first electrical signal at an input electrode in contact with a first set of porous, polymeric pads, wherein the first set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site," and "detecting the first electrical signal at an output electrode in contact with a second set of porous, polymeric pads, wherein the second set of porous,

polymeric pads comprises the porous, polymeric pad at the specific test site". Claims 65-75 depend from and include all limitations of Applicants' claim 64. Accordingly, Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 64-75 over Kayyem in view of Roberts be withdrawn.

Claims 1-63 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sosnowski et al. (U.S. Patent Number 6,051,380) in view of Roberts et al.

Sosnowski discloses an array of test sites, each having a metal site. A single externally-accessible electrode (or bond pad) is connected to each test site (see for, example, Sosnowski Fig. 3 and col. 23, line 46 - col. 24, line 12). So, for example, in Sosnowski's Fig. 3, 64 test sites are provided along with 64 electrodes - one for each test site. In a different embodiment (Sosnowski Fig. 6), test sites are separated from their electrode by a buffer solution (see col. 27, lines 19-31). In any case, each site has an individual electrode. Sosnowski discloses that the array is 'self-addressable'. By 'self-addressable', Sosnowski discloses that the device itself can select the potential of each electrode (and, accordingly, each microlocation) in order to attract or repel a certain binding entity (see col. 28, lines 14-59). The Examiner concedes that Sosnowski does not recite interdigitated input and output electrodes.

Roberts is discussed above.

In contrast, Applicants' claims 1 and 2 clearly recite "a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site" and "a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site".

The Examiner suggests it would have been obvious to one of ordinary skill in the art to modify the apparatus of Sosnowski et al. by interdigitating the output and input electrodes as taught by Roberts for the advantage of increasing signal detection.

As discussed above, to constitute a proper 35 U.S.C. §103 rejection, the cited reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §2142).

Applicants submit that Sosnowski and Roberts, taken alone or in combination fail to disclose all limitations of Applicants' amended claims 1 and 2 including "a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site" and "a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site".

output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site".

Further, even if motivation was found in the references to arrive at the combination suggested by the Examiner, and Applicants do not so concede, the combination would not result in the apparatus claimed in Applicants' amended claims 3 and 4. For example, Sosnowski discloses only one electrode per test site. By definition, then, two electrodes are not present to result in interdigitated input and output electrodes as recited in claims 3 and 4.

Claims 5-63 depend from and include all limitations of claims 1 and 2. Accordingly, Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 1-63 over Sosnowski in view of Roberts be withdrawn.

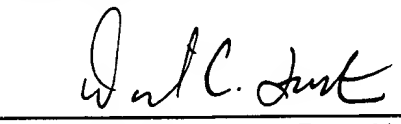
Applicant has added new claims 76-80 which further distinguish over the cited art. For example, Claims 76 and 77 recite electrodes embedded in the porous, polymeric pads. Claim 78 further requires that "each test site is uniquely indentified by two electrodes, a first electrode chosen from the set of input electrodes, and a second electrode chosen from the set of input electrodes". Claims 79 and 80 recite "x-y addressable" test sites. The cited art fails to disclose or suggest these features. Other of the added claims present other features that are neither disclosed nor suggested by the cited art.

CONCLUSION

Enclosed is our check to cover the cost of added claims not already paid for. While Applicant believes that no further fees are due at this time, the Commissioner is authorized to charge any fees that may be due as a result of filing this amendment, including additional claims fees not already paid for, or other fees that have not been separately paid, to Deposit Account 50-2319 (Order No. 469008-00137 [A-70203/RMS/AXG/JML]).

Respectfully submitted,

DORSEY & WHITNEY LLP

By 

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APPENDIX WITH MARKINGS SHOWING CHANGES MADE

Claims 1-4, and 64-68 were amended as follows:

1. (Amended) An apparatus for electrical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:

(a) a supporting substrate comprising an array of test sites,

(b) a plurality of porous, polymeric pads in contact with the supporting substrate at the test sites,

(c) a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged ~~to address a subset of the test sites~~ such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site,

(d) a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged ~~to address a subset of the test sites~~ such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site, and wherein each output electrode is in electrochemical contact with an input electrode,

(e) a plurality of linker moieties in contact with the porous, polymeric pads at the test sites,

(f) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules,

(g) a ~~means~~ signal generator for producing an electrical signal at each input electrode,

(h) a ~~means~~ detector for detecting changes in the electrical signal at each output electrode, and

(i) an electrolyte solution in contact with the porous polymeric pads, input electrodes, output electrodes, linker moieties, and probe molecules, wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.

2. (Amended) An apparatus for electrical or electrochemical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:

(a) a supporting substrate comprising an array of test sites,

(b) a plurality of porous, polymeric pads in contact with the supporting substrate at the test sites,

(c) a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged ~~to address a subset of the test sites~~ such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site,

(d) a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged ~~to address a subset of the test sites~~ such that a first portion

of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site, and wherein each output electrode is in electrochemical contact with an input electrode,

(e) a plurality of linker moieties in contact with the porous, polymeric pads at the test sites,

(f) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules,

(g) at least one reference electrode in electrochemical contact with the input and output electrodes,

(h) a ~~means~~ signal generator for producing an electrical signal at each input electrode,

(i) a ~~means~~ detector for detecting changes in the electrical signal at each output electrode, and

(j) an electrolyte solution in contact with the porous polymeric pads, input electrodes, output electrodes, linker moieties, reference electrode, and probe molecules, wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.

3. (Amended) An apparatus ~~for electrical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:~~according to claim 1, wherein

~~(a) a supporting substrate comprising an array of test sites;~~

~~(b) a set of input electrodes in contact with the supporting substrate, wherein each input electrode is arranged to address a subset of the test sites;~~

~~(c) a set of output electrodes in contact with the supporting substrate at the test sites, wherein each output electrode is arranged to address a subset of the test sites, each output electrode is in electrochemical contact with an input electrode, and~~ the output electrodes and input electrodes are interdigitated at the test site~~;~~.

~~(d) a plurality of linker moieties in contact with either the input electrodes, the output electrodes, or both the input electrodes and output electrodes at the test sites;~~

~~(e) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules;~~

~~(f) a means for producing an electrical signal at each input electrode;~~

~~(h) a means for detecting changes in the electrical signal at each output electrode, and~~

~~(i) an electrolyte solution in contact with the input electrodes, output electrodes, linker moieties, and probe molecules,~~

~~wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.~~

4. (Amended) An apparatus according to claim 2, wherein ~~for electrical or electrochemical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:~~

~~(a) a supporting substrate comprising an array of test sites;~~

~~(b) a set of input electrodes in contact with the supporting substrate, wherein each input electrode is arranged to address a subset of the test sites;~~

~~(c) a set of output electrodes in contact with the supporting substrate at the test sites, wherein each output electrode is arranged to address a subset of the test sites, each output electrode is in electrochemical contact with an input electrode, and~~ the output electrodes and input electrodes are interdigitated at the test site.;

~~(d) a plurality of linker moieties in contact with either the input electrodes, the output electrodes, or both the input electrodes and output electrodes at the test sites;~~

~~(e) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules;~~

~~(f) at least one reference electrode in electrochemical contact with the input and output electrodes;~~

~~(g) a means for producing an electrical signal at each input electrode;~~

~~(h) a means for detecting changes in the electrical signal at each output electrode, and~~

~~(i) an electrolyte solution in contact with the input electrodes, output electrodes, linker moieties, reference electrode, and probe molecules,~~

~~wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.~~

64. (Amended) A method for the electrical detection of molecular interactions between a probe molecule immobilized at a specific test site ~~in the apparatus of any of Claims 1, 2, 3, or 4~~ and a target molecule in a sample solution, comprising:

(a) applying a first electrical signal at an input electrode in contact with a first set of porous, polymeric pads, wherein the first set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site,

(b) detecting the first electrical signal at an output electrode in contact with a second set of porous, polymeric pads, wherein the second set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site,

(c) exposing the first and second sets of porous, polymeric pads to a sample mixture containing the target molecule,

(d) applying a second electrical signal at an input electrode in contact with the first set of porous, polymeric pads,

(e) detecting the second electrical signal at an output electrode in contact with the second set of porous, polymeric pads,

(f) comparing the first electrical signal detected in step (b) with the second electrical signal detected in step (e), and

(g) determining whether the first electrical signal is different from the second electrical signal.

65. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method selected from the group consisting of impedance spectroscopy, cyclic voltammetry, alternating current (AC) voltammetry, pulse voltammetry, square wave voltammetry, ~~AC voltammetry,~~ hydrodynamic modulation voltammmetry, conductance, potential step method, potentiometric measurements, amperometric measurements, and current step method~~, other steady-state or transient measurement methods, and combinations thereof~~.

66. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured over a range of frequencies.

67. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured by transient methods with AC signal perturbation superimposed upon a direct current (DC) potential applied to an electrochemical cell.

68. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured by impedance analyzer, lockin amplifier, AC bridge, AC voltammetry, or combinations thereof.

Claims 76-80 were added.